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Vaccination and RRT

CKJ Review

The ABC of pneumococcal infections and vaccination in patients with chronic kidney disease

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Abstract

Background. In the general population, pneumococcal polysaccharide vaccines (PPV) decrease the incidence of invasive pneumococcal disease (IPD) whereas the impact on the prevention of noninvasive pneumococcal disease is less clear. As compared with PPV, pneumococcal conjugate vaccines (PCV) provoke a higher, longer-lasting immune response resulting in a 45% decreased incidence in vaccine-type pneumonia, and a 75% decrease in vaccine-type IPD.

Methods. Literature review on pneumococcal vaccination in end-stage renal disease.

Results. As compared with the general population, patients with chronic kidney disease (CKD) suffer increased mortality and morbidity from pneumococcal disease (PD), being up to 10-fold for those treated with dialysis. Numerous, usually small and methodological heterogeneous studies demonstrate that PPV provokes a serological response in dialysis patients, kidney transplant recipients, children with nephrotic syndrome and CKD patients receiving immunosuppressive medication. This response is of less intensity and duration than in healthy controls. Similar observations were made for the PCV. The protective value of these vaccine-elicited anti-pneumococcal antibodies in the CKD population remains to be substantiated. For patients treated with dialysis, epidemiological data demonstrate a correlation—which does not equal causality—between pneumococcal vaccination status and a slightly decreased total mortality. Clinical outcome data on the effectiveness of pneumococcal vaccination in the prevention of morbidity and mortality in the CKD population are lacking.

Conclusions. Awaiting better evidence, pneumococcal vaccination should be advocated in all patients with CKD, as early in their disease course as possible. The ACIP schedule recommends a PCV-13 prime vaccination followed by a PPV-23 repeated vaccine at least 8 weeks later in pneumococcal non-vaccinated patients, and a PCV-13 vaccine at least 1 year after the latest PPV vaccine in previously vaccinated patients. In the UK, vaccination with PPV-23 only is recommended. There exist no good data supporting re-vaccination after 5 years in the dialysis population.

Keywords: antibody; dialysis; pneumococcal vaccination; prevention; transplantation

Background

In recent years, pneumococcal vaccination was a field in strong evolution. New conjugated vaccines were licensed, cohort data on the effect of vaccination on the epidemiology of PD emerged, new assays to evaluate vaccine efficacy were developed and one large population-based prospective study on the effect of pneumococcal vaccination (CAPiTA) was recently finished.

This review aims to give an update on pneumococcal vaccination in nephrological patients. The review starts with a brief overview of the evidence gathered in the general population and finishes with a summary of the available evidence in all groups of CKD patients.

Pneumococcal infections and vaccination in the general population

Definition, classification and burden of disease

Pneumococcal disease is every infection caused by the Gram-stain positive coccus *Streptococcus pneumonia* also

called the pneumococcus. The polysaccharide composition of the pneumococcal outer capsule distinguishes >93 serotypes that predispose for heterogeneous disease manifestations and a variable epidemiology across the world [1, 2]. Colonization of the upper respiratory tract, frequently occurring in early infancy, universally precedes infection [2, 3]. Tissue invasion is generally triggered by local inflammation as seen in the presence of viral infections and can be prevented when serotype-specific anticapsular antibodies with opsonophagocytic capacity are present [3, 4]. PD is classically divided into noninvasive and IPD.

Noninvasive pneumococcal disease. Noninvasive pneumococcal diseases are those infections where *S. pneumoniae* is only isolated from non-sterile body sites, such as sinusitis, acute otitis media and non-bacteraemic community-acquired pneumonia (CAP) [1]. Pneumococci cause about one-quarter of CAP, making CAP the highest burden of PD in adults [1]. The incidence of CAP is 1.6 to 11.6 per 1000 persons per year [1]. In the German CAPNETZ study, short-term mortality of pneumococcal CAP varied between 0.3% in young patients without comorbidity and 26.6% in elderly residing in a nursing home [5, 6]. In addition, an excess in mortality as high as 30–50% is observed within the 3–5 years following the survival of an initial episode of CAP [1].

Invasive pneumococcal disease. Invasive pneumococcal diseases are infections confirmed by the isolation of *S. pneumoniae* from a normally sterile body site, such as blood and cerebrospinal fluid. Consequently, incidence rates of IPD may vary considerably depending on differences in local practices in performing blood cultures. In a Belgian study, bacteraemic pneumonia, meningitis and primary bacteraemia without obvious focus consisted of respectively 79, 6 and 6% of the IPD in adults [7, 8]. Thirty-eight percent of IPD occurs in children younger than 2 years, and 54% in adults of >50 years [7, 9]. In adults, IPD incidence and mortality increase incrementally with age, ranging from 3.8/100 000/year for adults aged 18–34 years to 36.4/100 000/year for adults over 65 years of age [7, 9, 10]. Immunocompromised adults are at highest risk, with incidences of 186 and 173/100 000/year in adults aged 18–64 years with respectively hematological cancers and HIV [10]. IPD mortality ranges from 10 to 30% [1, 2]. Before the introduction of the pneumococcal polysaccharide vaccine (PCV), pneumococci were the third pathogen in bloodstream infections (after *Escherichia coli* and *Staphylococcus aureus*), with an incidence of 10/100 000/year [8].

Antibiotic treatment

Pneumococcae are used to be susceptible to all beta-lactam antibiotics, namely penicillins, cephalosporins and carbapenems [11]. A 2014 review found decreased penicillin susceptibility in 8.4–20.7% of the isolates, with major variability among countries [11]. High doses of penicillins generally remain active against penicillin-intermediate susceptible infections outside the meningeal compartment. Most isolates remain susceptible to third-generation cephalosporins and fluoroquinolones. Erythromycin resistance is high.

Prevention of pneumococcal infections with vaccination

How to evaluate the protective effect of a pneumococcal vaccine. A long-lasting, well-powered, prospective, randomized controlled trial (RCT) in the population at risk correlating vaccination with the subsequent risk for PD and all-cause mortality and morbidity is the most robust way to evaluate the efficacy of pneumococcal vaccination. The efficacy of the PCV-13 in the elderly has been investigated according to these requirements in a large RCT known as the CAPiTA trial [12, 13]. A smaller RCT investigated the efficacy of PPV-23 against pneumonia and mortality in the high-risk subpopulation of elderly residing in a nursing home [14].

Investigators, however, frequently rely on less-robust methods such as observational studies (case–control and cohort) and trials with surrogate endpoints such as the *in vitro* evaluation of the vaccine immunogenicity [4]. These *in vitro* methods are, however, diverse and poorly standardized [4, 15]. Older radioimmunoassays (RIA) are hard to interpret due to their inability to distinguish non-neutralizing common cell-wall polysaccharide antibodies from neutralizing capsular-polysaccharide-specific antibodies. Serotype-specific enzyme-linked immunoabsorbent assays (ELISA) selectively quantify these neutralizing, capsular-polysaccharide-specific antibodies. Opsonophagocytosis assays (OPA) provide functional information on the protective effect of serospecific antibodies [15]. ELISA and OPA assays correlate well in young children, but poorly in the elderly and in immunocompromised patients [15]. The serological cutoffs for protection are poorly defined.

The pneumococcal polysaccharide vaccine. The 14-valent polysaccharide vaccine (PPV-14) was FDA-approved in 1977, and the 23-valent (PPV-23), containing surface polysaccharide of serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F and 33F, in 1983 [2]. PPVs induce a B-cell response that wanes within 5 years but remains detectable for >10 years [2, 16].

Data on clinical efficacy of the PPV, summarized in a 2013 Cochrane analysis, demonstrate a protective effect in reducing IPD in adults, which is less clear in immunocompromised and chronically ill patients [17]. PPV provides protection against presumptive pneumococcal pneumonia [OR = 0.46 (0.25–0.84)], but the evidence for a protective effect against all-cause pneumonia is inconclusive [17]. The PPV-23 is poorly immunogenic in infants and consequently not licensed for under the age of 2 [2]. Most guidelines recommend the PPV-23 for the prevention of IPD in all adults aged ≥65 years, and for adults at risk for pneumococcal infections aged 19–64 years [10, 18, 19]. Despite the lack of clinical data and inconclusive immunogenicity studies, a re-vaccination after 5 years is generally recommended [2].

The pneumococcal conjugate vaccine. In the conjugate vaccine, the pneumococcal polysaccharide antigen is conjugated to a protein to enhance immunogenicity, being either protein D, diphtheria toxoid and tetanus toxoid carrier proteins for the PCV-10 or the CRM 197 carrier protein for the PCV-7 and PCV-13 [2]. Conjugate vaccines elicit a specific B-cell and a T-helper-2 cell response and induce immunological memory [2]. Conjugate vaccines are also immunogenic in younger children and

immunocompromised adults [2]. The PCV-7 (including serotype 4, 6B, 9V, 14, 18C, 19F and 23F) was FDA-approved in 2000. The PCV-13 (additionally covers serotypes 1, 3, 5, 6A, 7F and 19A) nowadays replaced [20] the PCV-7 [1]. Prior vaccination with the PPV negatively affects the antibody response to subsequent conjugated vaccines, an effect that is not restored by adding additional doses of conjugated vaccine [21]. Consequently, a PCV prime–PPV repeat vaccination (to enhance the number or serotypes) strategy is recommended [13, 21].

Effectiveness of the conjugate vaccine on the population level.

The Dutch CAPiTA trial is a prospective, double-blinded, placebo-controlled RCT, investigating the efficacy of PCV-13 in ∼85 000 adults older than 65 years without known immunodeficiency [12, 13]. The CAPiTA trial demonstrates a highly significant 45.6% [95% CI (21.8–62.5)] reduction in first episode of vaccine-type CAP, a 45.0% [95% CI (14.7–65.3)] reduction in first episode of non-bacteraemic/noninvasive vaccine-type CAP and a 75% [95% CI (41.4–90.8)] reduction in first episode of vaccine-type IPD, with, however, no effect on overall mortality [12].

Epidemiological data after the introduction of universal PCV-7 vaccination in childhood in the UK demonstrate a 98% reduction of vaccine-type PD in children younger than 2 years, and of 81% in adults over 65 years [22]. Non-vaccine-type disease however increased, respectively, 68 and 48% in children and adults over 65 years, a phenomenon called serotype replacement [1, 22]. The net overall reduction in IPD was 56% in children and 19% in adults over 65 years [22]. The introduction of conjugated pneumococcal vaccines not only reduced IPD incidence in vaccinated but also in unvaccinated persons [1, 22–24]. This phenomenon is called the 'herd protection' and a consequence of a reduced nasopharyngeal colonization in the population [1, 22–24].

Safety of pneumococcal PPV and PCV vaccine. Polysaccharide and conjugated pneumococcal vaccine have a comparable and high safety profile, with regular local irritation at the injection site (pain, redness, swelling and limitation of movement of the injected arm), and rarely systemic side effects such as fatigue and headache [10, 13].

Pneumococcal vaccination in adults: 2013 UK and France, and 2014 USA and Spanish recommendations. In the USA (provided by the 'Advisory Committee on Immunization Practices' or ACIP) and Spain, PCV-13 followed by a PPV-23 repeated dose 6–12 months later (and at least 8 weeks later) is recommended for all adults of ≥65 years old, and in adults of ≥19 years old with immunocompromising conditions, functional or anatomic asplenia, cerebrospinal fluid leaks or cochlear implants [10, 13, 20]. A second PPV-23 repeated dose vaccination may be given at least 5 years later [10, 13, 20]. Immunodeficiency is defined as congenital or acquired immunodeficiency, HIV, haematological malignancies, generalized malignancy, immunosuppressive treatment, solid-organ transplantations, CKD and nephrotic syndrome [10, 13]. In previously PPV-vaccinated persons, a PCV-13 should not be given before 1 year after the latest PPV vaccine [13, 20]. Pneumococcal vaccination can be co-administered with trivalent inactivated influenza vaccination [13].

The 2013 French recommendations endorse the ACIP PCV-13 prime–PPV-23 boost strategy for immunocompromised patients, while still advocating a PPV-23 prime vaccine in non-immunocompromised persons of ≥65 years [19]. The 2013 British NHS recommendations define a similar target population but only recommend the PPV-23 vaccine in adults [18].

Cost-effectiveness of pneumococcal vaccination. In 2012, the CDC estimated the efficacy of PCV-13 in reducing IPD and pneumonia to be respectively 75 and 13% in adult HIV/AIDS and dialysis patients [10]. According to these data, health costs could be reduced by 7.6 million dollars, 1360 quality-adjusted life years (QALY) could be gained and 57 cases of IPD could be avoided by implementing the ACIP guidelines in the USA [10].

A 2014 systematic review of available European studies on cost-effectiveness of PCV-13—which does not yet include the CAPiTA data—concluded that, given the limited information and the great variability within and between studies, no clear conclusions could yet be drawn on the economical utility of conjugate pneumococcal vaccination for the entire population or in pre-defined (immunocompromised) subpopulations [25].

Immune dysfunction in CKD

CKD is associated with hypercytokinaemia and ongoing inflammation, predisposing for cardiovascular disease [26]. CKD also results in a decreased innate and adaptive immune response, predisposing for infections [26, 27]. Disturbances of innate immunity results in inadequate monocyte and neutrophil function and persistent low-grade inflammation [26, 27]. Disturbances of the adaptive immune responses result in a decrease in antigen presenting function, T-cell-mediated immune response and immunological memory [26, 27]. Consequently, CKD patients are prone to vaccine hyporesponsiveness, which increases with more advancing stages of CKD, and with concomitant malnutrition and immunosuppressive treatment [26–29]. It thus seems logical to vaccinate CKD patients as early as possible in the course of their disease [27, 28].

Pneumococcal infections and vaccination in patients with CKD

Search strategy

A Pubmed search was performed in September 2014 using the terms (pneumococcal vaccine) and (end-stage renal disease) or (CKD) or (dialysis) or (transplantation) as well as a search of the relevant references. All papers providing data on epidemiology, safety and efficacy of the pneumococcal vaccine in CKD were included. This resulted in 2 papers on epidemiology of pneumonia, 2 papers on the epidemiological effect of vaccination, and 5 trials on pneumococcal vaccination for CKD; 2 systematics reviews and 2 additional papers covering 14 trials for transplant recipients, and 1 systematic review and 5 additional trials for patients with nephrotic syndrome. The results are summarized in Table 1.

Table 1. Evidence supporting the use of pneumococcal vaccination in patients with CKD and dialysis, kidney transplant recipients and in patients receiving immunosuppressive medications

Levels of evidence	CKD and dialysis	Transplant	Immunosuppressive medication
1. Randomized controlled trials	*No data*	*No data*	*No data*
2. Retrospective epidemiological cohort studies	6–16% lower overall mortality [30, 31]	*No data*	*No data*
3. Serological data			
• Polysaccharide vaccine	Response in ±80%, waning over time [4, 32–35]	Response in ±80–90%, waning over time [4, 36, 37, 38]	'Reduced response' [36, 39–41]
• Conjugated vaccine	*No data*	Response in ±77%, waning over time% [4, 36–38]	'Reduced response' [39, 36, 40, 41]
Serotype coverage in the population at risk [7, 10, 42]			
1. PCV-13		50–64%	
2. PPV-23		Additional 20–25%	

Patients with CKD and immunosuppressive conditions or medication

General considerations

Data on the immunogenicity, effectiveness and safety of PPV23 and PCV vaccination in immunocompromised patients are limited since immunocompromised patients are typically excluded from pre-licensure studies, and post-licensure studies usually include smaller groups of patients with heterogeneous immune-compromising conditions (e.g. transplantation, vasculitis and malnutrition) [36, 39]. Consequently, vaccination recommendations for immunocompromised patients are mainly extrapolated from what is known in healthy persons [36].

High-level immunosuppressive conditions occur in the first 2 months after solid-organ transplantation, HIV with <200 T4 cells, cancer chemotherapy and treatment with ≥20 mg prednisolone equivalents for ≥14 days or immune modulators such as TNF-α blockers and rituximab [39].

Vaccination guidelines recommend that specialists who care for immunocompromised patients take responsibility for adequate vaccination [39]. Inactivated vaccines, such as the PCV13 and PPV23, should be administered at least 2 weeks prior to immunosuppression, but vaccination should never delay the initiation of essential immunosuppression [39]. All candidates for solidorgan transplantation should receive pneumococcal vaccination early in their disease [39].

Serotype coverage in immunocompromised patients by the PCV-13 and PPV-23

In the USA, in 2010 (10 years after the introduction of the PCV-7), 50% of IPD among immunocompromised adults were caused by serotypes included in the PCV-13, and an additional 21% by serotypes only contained in the PPV-23 [10]. In a Spanish survey between 1996 and 2010, 64% of IPD was covered by the PCV-13, and the risk for non-coverage of either the PCV-13 or the PPV-23 was the highest for immunocompromised patients [43]. In a Belgian survey on IPD in adults between 2009 and 2011 (2 years after the introduction of PCV-7), 61% of serotypes were covered by the PCV-13, and an additional 25% by the PPV-23 [7]. Predisposing conditions for IPD were present in 85% of the patients aged 65 years or older, being renal failure in 19% and immunosuppressive medication in 14% [7]. Continuous surveillance remains mandatory since serotype replacement may cause a decreased serotype coverage in the future.

Efficacy and safety of pneumococcal vaccination in immunocompromised patients

Inactivated vaccines apparently have a similar safety profile but reduced efficacy in immunocompromised patients [39–41]. This has been demonstrated for the inactivated trivalent flu vaccine in rheumatological patients receiving azathioprine, rituximab or infliximab, and for the PPV in patients with rheumatoid or psoriatic arthritis receiving methotrexate or rituximab, but not anti-TNF-α treatment [39–41, 44, 45]. In an RCT comparing the immunogenicity of PCV-7 and PPV-23 in frail, hospitalized elderly, there was no clear benefit of one vaccine over the other, and the ability of both vaccines to elicit an immune response was strongly negatively affected by frailty [46]. Vaccination does not trigger disease flares for systemic lupus erythematous or vasculitis, or rejection in solid-organ recipients, and should thus not be withheld for this reason [39].

CKD patients with kidney transplantation

Two reviews [4, 36] summarized 12 trials on pneumococcal vaccination in renal transplant recipients published before the end of 2011, and 2 additional trials were published after 2011 [37, 38]. These trials were heterogeneous in vaccination schedule (7 including 372 patients and 98 controls using PPV-14; 4 including 118 patients using PPV-23; and 3 including 119 patients using various PCV-7-based regimens, either or not with PPV-23 boosting), patient population (adult or children, with only 5 trials using controls) and assays and definitions used for serological evaluation (with older non-specific RIA assays used in more than half of the trials) [4, 36]. Serological vaccine response did not differ significantly from that observed in the general population, although the height of antibody titres tended to be lower, and the decline in antibody titre faster [4, 36], especially in the elderly, and in those patients receiving tacrolimus instead of cyclosporine or with an impaired kidney function [38]. As compared with a single vaccination with PPV, a PCV-7 prime vaccination with a PPV-23 repeated dose after 1 year did not enhance immune response [37]. These trials suggest a beneficial effect of pneumococcal vaccination in renal transplant recipients by electing an increase in antibody titre against at

least a part of the serotypes without revealing harm; they do not yet prove clinical benefit. There are no RCTs with morbidity or mortality endpoints assessing the efficacy of pneumococcal vaccination in renal transplant patients.

CKD patients with nephrotic syndrome

All data on pneumococcal vaccination in patients with nephrotic syndrome are derived from trials with serological endpoints in children. There exist no data in adults, nor epidemiological data or clinical trials linking pneumococcal vaccination with outcome.

In children with nephrotic syndrome, PPV and PCV vaccine was safe and provoked a good short-term serological response unless the patients received cyclophosphamide or other immunomodulatory medications [4, 47–51]. At the long term, a considerable decline in antibody titres was observed, especially in those infants with ongoing disease [4, 47, 51]. A PCV-7 repeated dose vaccination could provoke a significant increase in sero-titres, especially if not under treatment with immunomodulatory medications [50].

Patients with end-stage renal disease treated with dialysis

The risk for pneumococcal infections in patients with end-stage renal disease

Mortality is much higher in patients with end-stage renal disease (ESRD) than that in the general population, ranging from 63 times higher for those under 25 years to 7 times higher for those over 75 years old [52]. Infections are the second leading cause of death in ESRD after cardiovascular disease [53]. Infectious mortality is 21.3/1000 patients years, caused by sepsis and pulmonary infections in respectively 75 and 20% [53, 54]. Pneumonia incidence in dialysis patients is 27.9/100 person-years, with a 1-year survival rate of only 0.51 [55]. As compared with ESRD patients without pneumonia, pneumonia increases mortality 4.99- and 2.12-fold in respectively the subsequent 6 months and 5 years [55]. An episode of pneumonia also increases the risk for cardiovascular events 3.02- and 1.45-fold during respectively the subsequent 6 months and 5 years [55]. Crude pneumonia mortality in ESRD patients is ∼10- to 16-fold higher than that in general population [54, 55].

Efficacy of pneumococcal vaccination in patients with ESRD

Circumstantial evidence from epidemiological data

Two retrospective cohort studies in the USA including respectively 118 533 haemodialysis patients surviving 2 years on haemodialysis and 36.966 patients surviving 1 year on haemodialysis demonstrated a hazard rate for mortality of 0.84 [30] to 0.94 [31] for pneumococcal vaccination alone and 0.71 [30] to 0.73 [31] for combined pneumococcal and flu vaccination. This beneficial correlation does not prove causality. It may also be a consequence of e.g. the correlation of higher vaccination rates and a better overall quality of care [31], or a higher patients' self-involvement in the management of their sickness [30]. Moreover, almost half of the haemodialysis patients aged over 65 years do not survive for 2 years [52]. Overall, pneumococcal vaccination rates in the dialysis population range from 21 to 41.8% [30, 31].

Evidence derived from trials with serological endpoints

Data on the serological efficacy of pneumococcal vaccination in dialysis patients are scare. Until 2004, nine vaccination studies using the polysaccharide vaccine (PPV-14 in six, PPV-23 in three) were performed in ESRD patients whether or not treated with dialysis [4]. The trials were nonrandomized, antibodies were measured with non-specific RIA assays, the number of patients included was small (average 16.7, range 10–33) and the follow-up usually limited to 6 to 12 months [4]. Overall, a serological response to at least some of the serotypes was documented in the majority of patients, which tended to be lower and more rapidly waning than that in healthy controls [4]. In the only study providing longer follow-up, 7 of 33 patients vaccinated with the PPV-14 developed IPD over a 5-year period [32]. This was confirmed in two more recent trials with the PPV-23, documenting hyporesponsiveness with associated increased risk for pneumococcal infections in one-fifth (14 of 66) of the patients [33, 34]. Revaccination after 2 years with the PPV-14 in 17 previously vaccinated patients provoked a two-fold increase in antibody levels [35]. The only trial with the conjugated PCV-7 vaccine in 48 children demonstrated an antibody level of ≥0.35 μg/mL against at least one serotype in all patients [56]. However, more than half of the patients did not respond with a more than 4-fold rise in antibody levels for at least five serotypes [56].

Evidence derived from trials with morbidity and mortality endpoints

There exist no well-powered studies on the effect of pneumococcal vaccination on morbidity and mortality in patients treated with dialysis.

Conclusions

In the general population, the PPV decreases the incidence of IPD, and pneumococcal type pneumonia. The conjugated pneumococcal vaccine provokes a stronger and more long-lasting immune response than the polysaccharide vaccine. PCV efficacy in reducing vaccine-type pneumonia and IPD in adults has recently been demonstrated. However, due to serotype replacement, only 50–64% of the serotypes involved in IPD in immunocompromised patients were covered by the PCV-13 after the introduction of universal PCV vaccination in children. This figure may further decline due to the reduction of circulating vaccine serotypes by interfering with nasopharyngeal colonization, serotype replacement and herd immunity effects.

For CKD patients treated with dialysis, epidemiological data demonstrate a lower mortality in patients vaccinated with the (polysaccharide) pneumococcal vaccine, especially if they were also vaccinated against flu. This correlation does not, however, prove causality. Efficacy data on pneumococcal vaccination in CKD patients are mainly derived from smaller studies with serological endpoints.

Pneumococcal vaccination (either PPV or PCV) seems to elicit an increase in antibody titres in all subgroups of CKD patients, that is, however, less pronounced and less long-lasting than that in the general population. Clinical outcome dates in CKD patients are lacking.

Currently, there is no solid evidence supporting the recommendations to administer CKD patients a pneumococcal vaccination. On the other hand, the burden of pneumococcal infections in CKD patients is high, the cost of pneumococcal vaccination is low as compared with the global health costs in this population and there are no data indicating potential disadvantages. Awaiting better evidence, all CKD patients should receive pneumococcal vaccination, either in a PCV-13 prime–PPV-23 boost schedule, or with only a PPV-23 prime vaccination. The potential advantage of a re-vaccination after 5 years may be nullified by the limited life-expectancy of most dialysis patients.

Conflict of interest statement. None declared.

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